

REMARKS/ARGUMENTS

Reconsideration of this application is requested. Claims 3, 4, 8-11, 16, 19, 22 and 23 are in the case.

I. THE OBVIOUSNESS REJECTION

Claims 3, 4, 8-11, 16 and 19 stand rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Friedlos *et al.*, *J. Med. Chem.* 1997, 1270-1275 (Friedlos) in view of Patani *et al.*, *Chem. Rev.* 1996, 3147-3176 (Patani). That rejection is respectfully traversed.

In response, and without conceding to the rejection, claims 4 and 8 have been further amended in the definition of Y in formula IIIb to exclude CONH₂ as a possible value for Y. This has been effected by adding the words "other than CONH₂" after both "CONHR₂" and "CONR₂R₃" in the definition of Y in both claim 4 and claim 8. Support is provided by the fact that there are compounds of formula IIIb disclosed where Y is not CONH₂. No new matter is entered by requesting the exclusion of compounds where Y is CONH₂.

The effect of the requested amendment to the definition of Y is to require one of ordinary skill in the art to contemplate a yet further modification of the compounds of Friedlos in order to arrive at or render obvious the compounds as now claimed. In particular, all relevant compounds described in Friedlos have CONH₂ as the value for R (equivalent to Y in formula IIIb). This includes the sole asymmetric compound (compound 6), as well as all of the compounds described in Friedlos as having activity sufficient to merit further investigation (compounds 8, 9, 13 and 14).

There would have clearly been no motivation to one of ordinary skill based Friedlos to develop compounds in which R is not CONH₂. Compounds in which R is other than CONH₂ suffer in comparison with their analogs in which R is CONH₂. For example, if the potency of compounds 15 and 16 (in which R is CONHCH₂CHOHCH₂OH) is compared with compounds 12 and 14 in which R is CONH₂, it is clear that compounds 15 and 16 have reduced potency. The same trend is seen if compounds 10 and 11 (in which R is again CONHCH₂CHOHCH₂OH) are compared with compounds 4 and 9 respectively (in which R is CONH₂). Reference is made in particular to the IC₅₀ values against T79-A3 for these compounds.

The compounds as now claimed are therefore a further structural modification away from the Friedlos compounds referred to in the Action. The compounds in Friedlos most directly relied upon in the Action are compounds 6 and 13. The bromomesylate compounds of formula IIIb now claimed have two structural differences over compound 13 of Friedlos, and three structural differences over compound 6 of Friedlos. There would clearly have been no motivation to one of ordinary skill based on Friedlos, either taken alone or in combination with Patani, to make such double or triple structural changes and to modify the compounds of Friedlos in the manner now required by the claims of the present application.

Absent any motivation to arrive at the invention as now claimed, it is clear that Friedlos and Patani, either when taken singly or in combination, do not give rise to a *prima facie* case of obviousness. Withdrawal of the obviousness rejection is therefore respectfully requested.

II. CLAIM AMENDMENTS

As noted earlier, claims 4 and 8 have been amended in the definition of Y in formula IIIb in order to exclude CONH_2 as a possible value for Y, by adding the words "other than CONH_2 " after both " CONHR_2 " and " CONR_2R_3 " in the definition of Y in both claim 4 and claim 8. In addition, new dependent claim 22 has been added to define Y as " CONHR_2 where R_2 is $\text{C}_1\text{-C}_6$ alkylene substituted with hydroxy" and new claim 23 has been added to define Y as " $\text{CONHCH}_2\text{CH}_2\text{OH}$ " specifically. No new matter is entered.

Favorable action is awaited.

Respectfully submitted,

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